UNIVERSIDAD AUTÓNOMA DE NUEVO LEÓN
FACULTAD DE INGENIERÍA MECÁNICA Y ELÉCTRICA

TESIS

POTENTIAL IMPACT OF IMPLEMENTING A KIDNEY EXCHANGE PROGRAM IN MEXICO: CASE STUDIES FROM MEXICAN DATA BASES

POR

YESSICA REYNA FERNÁNDEZ

COMO REQUISITO PARCIAL PARA OBTENER EL GRADO DE MAESTRÍA EN CIENCIAS EN INGENIERÍA DE SISTEMAS

SEPTIEMBRE, 2019

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SUBDIRECCIÓN DE ESTUDIOS DE POSGRADO

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Subdirección de Estudios de Posgrado

Los miembros del Comité de Tesis recomendamos que la Tesis "Potential Impact of Implementing a Kidney Exchange Program in Mexico: Case Studies from Mexican Databases", realizada por el alumno Yessica Reyna Fernández, con número de matrícula 1525016, sea aceptada para su defensa como requisito parcial para obtener el grado de Maestría en Ciencias en Ingeniería de Sistemas.

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Contents

List of Figures

List of Tables

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Abstract

Yessica Reyna Fernández.

Candidato para obtener el grado de Maestría en Ciencias en Ingeniería de Sistemas.

Universidad Autónoma de Nuevo León.

Facultad de Ingeniería Mecánica y Eléctrica.

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The need to promote a donation culture in México has become of vital importance, given that the waiting list for organ transplantation grows faster than the number of patients that receive a transplant each year. People with end-stage renal disease are anxious to get a kidney transplant; this kind of treatment is the most economical one given the high cost of dialysis.

Through the use of real data, we want to show the impact and benefit of kidney exchange programs, illustrating how can a kidney exchange program could be carried out in the state and in the country and its consequences on people's lives by improving their quality of life by reducing their time in the waiting list It is worth mentioning that such programs have already been successfully implemented in other countries.

In the kidney exchange problem, when modeled as a graph, incompatible pairs of patient-donor are considered as nodes, and the edges reflect the compatibility with other pairs, with the donor of a pair donating his/her kidney to the patient in another pair, and so on. Usually, the donors are family members or very close friends. In some cases, there is an extremely generous person, so-called altruistic donor, who decides to donate a kidney to anyone in need. When such donors exist, we can make two different considerations regarding the mechanism of matching between donor and recipient.

A *cycle* is an ordered list of pairs of patient-donor, such that one incompatible pair donates a kidney, and another incompatible pair receives a kidney, and so on, until the last incompatible pair donates a kidney to the first pair that started the donations. A pair is assigned to at most one cycle. A *chain* is an ordered list of pairs of patient-donor in which the donations are started by an altruistic donor giving his/her kidney to a patient in an incompatible pair. The next pair received a kidney provided by an already benefited pair. This succession of donations continues until it breaks the pattern or the next donation is made to the waiting list.

The kidney exchange problem (KEP) is a combinatorial optimization problem. Given a graph of compatibilities between incompatible pairs and/or with altruistic donors, find cycles and/or chains of maximal cardinality. We consider different experiments, analyzing the impact of the implementation of kidney exchange programs under different scenarios. The following three databases in the state of Nuevo León are considered:

- A waiting list from *Coordinación de Trasplantes de Órganos y Tejidos* (state) that includes small private hospitals and public hospitals from the state with 1086 patients.
- A waiting list from the San José Hospital (local) with 35 patients.
- A waiting list from the Dr. José Eleuterio González University Hospital (local) with 15 patients.

These databases have relevant information about each patient, mainly blood type to establish the compatibility of blood types. Because the information about the living donor of each patient is strictly confidential, in this study, the living donors are simulated according to the blood type distribution of the Mexican population.

The computational results show a tremendous positive impact of the implementation of a kidney exchange program on the state population. This result was expected since in other countries kidney exchange programs have had a significant positive influence. Another interesting observation is that as the size of the database increases so does the proportion of people who benefit from kidney exchanges.

The main contribution of this thesis is a full assessment of the real impact of a kidney exchange program in México and particularly in Nuevo León, as well as obtaining real data from different institutions and providing a real succession of transplants that can currently be carried out.

Firma del director: ______________________

Dr. Roger Z. Ríos Mercado

Chapter 1

Introduction

Kidney failure, also called end-stage renal disease (ESRD), is the last stage of a disease in which your kidneys fail, meaning that they do not work well enough for the person to survive without dialysis or a kidney transplant.

Currently, in México, there are a lot of people waiting for a kidney transplant. Commonly this takes several years, making that the majority of people are already dead before this ever happens. In 2018, 15,072 people were registered in the nation-wide waiting list [8], as for this same year only 3048 transplants were reported this causing that more than twelve thousand people keep waiting for a transplant for one more year, actually this list has grown considerably and for this moment in middle of 2019 has 17,367 people waiting for a kidney transplant.

Taking those information, if for every patient waiting to have a transplant there exists one person willing to donate, even when they may be no longer compatible or not be compatible since a begin, there is a possibility of searching for another donor, and considering that this could be affecting not only to this pair of persons but to many other too; then if we gather all this persons and search among them we could create new pairs between all the persons needing of a transplant and the donors to create good matches that benefits the most people possible.

The matching in a kidney exchange program can be differentiated in two ways, *cycles* and *chains*. Cycles are ordered lists of patient-donor pairs (PDPs) $(pd_1, pd_2, ..., pd_n)$ where every donor of pair pd_i points or gives his/her kidney to patient of pair pd_{i+1} [29]. The actual surgeries of the related resulting matchings are performed simultaneously to avoid unwanted incompatibilities between the persons involved, forming what we call a cycle, and where each patient cannot be involved in more than one cycle.

From a different point of view, a person that is willing to donate an organ without any reward is called an altruistic donor, someone not associated with the patient but willing to donate a kidney to someone in need. With the introduction of this type of donor, we have non-directed (ND) exchanges. In these exchanges, an altruistic donor gives his kidney to a patient that is on a kidney exchange program, and the recipient's donor gives his kidney to the next patient that is compatible on the waiting list or is directed to the deceased donor waiting list and creates what we call a chain; the exchange starts with an altruistic donor and continues pointing to the next pair of patient-donor, with donor of a given pair points or gives his/her kidney to the patient of the following pair in the chain, until the chain is broken or the donation is directed to the list of deceased people.

There are records of these types of procedures that have been carried out in México. A clear example of this is the first kidney exchange performed on living donors realized in the Juarez Hospital in México [7]. In this case, the donor was incompatible with his loved ones because of not having the same blood type. When a match is found, the corresponding patient is removed from the waiting list. As more matches are found, the waiting lists evidently becomes shorter and so does the waiting times for the remaining patients in the list.

1.1 Motivation

Kidney exchange is not a new topic around the world. Many countries have studied how they can innovate kidney exchange programs that are already implemented. Some organizations working on these programs in the USA are the following:

1. **OPTN/UNOS Kidney Paired Donation Program[1].** Having the mission and vision that every kidney transplant with an incompatible but willing and approved living donor receives a living donor kidney transplant, they developed a successful kidney paired donation (KPD) program with universal access to all members of the Organ Procurement and Transplantation Network (OPTN), which prioritizes the medical and psychosocial safety of living donors and candidates.

2. **UCLA Kidney Exchange Program[2].** It is a program that for more than 50 years has been a national leader in both clinical research and academic excellence, performing more than 300 transplantations each year.

3. **Alliance for Paired Donations.**[3] Their mission is straightforward, namely to save lives by securing a living donor kidney transplant for every patient who needs one.

In México, there are no kidney exchange programs to the best of my knowledge. The statistics for the country are as follows:

1. In 2018, 15,072 patients were on the waiting list [8].

2. México performed only 3,048 transplants in 2018 [6].

[1] United Network for Organ Sharing [US]. Kidney paired donation - UNOS. https://unos.org/transplant/kidney-paired-donation/

[2] UCLA Health. UCLA Kidney Exchange Program. Los Angeles, CA. https://www.uclahealth.org/transplants/kidney-exchange

[3] Alliance for Paired Kidney Donation. https://paireddonation.org/

3. The growth in the last ten years of living donations of kidneys is merely 11%.

As such programs have a huge boom in other countries and because of the need for such programs, we hope that with this study we can develop a program that provides guidelines for transplants with the information that is already available for the state and the country.

With the implementation of a kidney exchange program in México or only with the use of this scheme in each hospital, the waiting list would diminish and the quality of life of the patients would improve, together with a substantial reduction in treatments for their disease.

1.2 Objectives

- To obtain real information about patients on the kidney waiting list.
- To provide a full assessment of the potential impact of establishing a kidney exchange program based on real-world data of Mexican hospitals and institutions.
- To evaluate kidney exchange programs under different scenarios depending whether cycles and/or chains are allowed.
- To solve and show actual solutions of current databases by means of developing specific case studies.

1.3 Contribution

The idea of a kidney transplant for the people on the waiting list may feel so far away from reality because in México the waiting list keeps increasing every year. The main problem in México regarding kidney transplantation is not having a kidney exchange program as in other countries, affecting many sick people in need of a transplant.

With the introduction of the recompiled information of the incompatible pairs in México and including those rare cases in which an altruistic person is willing to donate a kidney, there would be a good basis for starting a well-implemented kidney exchange program, giving a life opportunity to all the persons currently on the waiting list.

In this thesis, we conduct a case of study on the implementation of a kidney exchange program in México. We use information about patients on the waiting list and about patients in hemodialysis in different institutions in Nuevo León, such as San Jose Hospital, Dr. José Euleterio Gonzalez University Hospital, and all the public clinics and small private hospitals of the state. In addition, we use the available information of the Centro Nacional de Trasplantes (CENATRA).

The main contribution of this thesis is the assessment of the potential impact of having a kidney exchange program in México based on experiments carried out on real-world databases.

The objective of the experiments is to show the real impact of implementing this kind of program in México or, more realistically, in Nuevo León, assuming availability of living donors. The results show the tremendous positive impact of kidney exchange programs in Mexican soil.

Chapter 2

Background

2.1 From Kidney Transplant to a Kidney Exchange Program

Like any other disease, kidney disease can be temporary or can start with the symptoms of chronic kidney disease (CKD) that are involved in end-stage renal disease, in which the affected person needs a transplant to survive [2]. It is reported [27] that even in the US, a country with years of experience implementing kidney exchange programs, 3971 patients died while they were on the waiting list expecting a transplant in 2004.

When a patient has end-stage renal disease, there are only two treatment options left: (1) constant dialysis treatment, which finally ends with the need for a transplant, a treatment that becomes very expensive over time; (2) a transplant, which is a cheaper treatment and the best option for the patient.

The treatment of hemodyalisis can keep a patient alive despite his renal failure. This process is carried out by the use of an artificial kidney, which is a machine that purifies the human blood, which is the normal function of the kidney every day. This treatment has been improved since it was first used for the control of renal disease.

A problem that can affect a patient when he is considering undergoing a transplant is the incompatibility that can exist between the patient and the potential donor. In [21] it is shown that in the United States in 2004, 30% of living donors (persons willing to donate a kidney to a recipient with end-stage renal disease) were biologically unrelated with their recipient because of the ABO blood type or a crossmatch incompatibility affecting the direct donation. Another factor that affects the donation is the time that the patient is on the waiting list, making him sicker and losing the opportunity to have the next kidney available from a cadaveric donor (a kidney donation from a deceased donor).

In other words, the donated kidney can come from a person who died and decided to donate his/her organs and whose kidney is healthy. The kidney can also come from a living person because studies have shown that a person can live with only one kidney. A person who has died and donated a kidney is called a deceased donor [20]. A living donor is a person who decided to donate one of his/her kidneys. This person can be a blood relative such as a parent, brother, or sister or may be a non-blood relative, such as wife or a husband; in some cases, this is a friend or even a stranger willing to donate.

One problem that can occur once the transplant has been performed is *rejection*. It can occur when a person that received a transplant, even when it was a successful surgery, creates antibodies against the new tissue, such that it starts to lose functionality and the organ is rejected.

This kind of exchanges these days come from swaps between incompatible donors and recipients for obtaining a compatible donor. These markets are examples of *barter exchanges*; a barter exchange is a swap between agents (for this thesis, patients) that are seeking to swap some items (the incompatible donors) with each other. The swap is made with cycles of these agents, with each agent receiving an item of the next agent in the cycle.

There are many examples of barter exchanges in history:

- Book exchanges in which people are interested to obtain new books to read.
- Car exchanges with the objective of obtaining a better car.
- House exchanges for holidays or vacations, among others.

For many years, these exchanges occurred for the needs of people around the world. For example, when they went on vacation and wanted to stay in a place that was cheaper than a hotel, also giving them the proper privacy, they got the idea of exchanging their house with another family in the place they wanted to go to.

This problem can be seen as a directed graph $G = (V, E)$ where the set V of vertices represents the agents of the problem and the set E is the weight of the edge from an agent v_i to another agent v_j if agent v_i wants an item from v_j. A cycle c is in this context a swap of items, obtaining an item from the next agent, and the weight denoted with w_c is the sum of the weights of the edges. We define an *exchange* as a collection of disjoint cycles, with the weight of the exchange being the sum of all cycles weights, and trying to obtain the maximum benefit.

In order to achieve the maximum benefit, we need to introduce another type of problem, the *clearing problem* [1], in which the goal is to find a maximum-weight exchange that consists of cycles of length at most a given constant k. This constant must be small because of the logistical constraints on the facilities and human resources in the hospital that are responsible for performing the transplants. Any k-cycle requires at least $2k$ resources, from doctors to operating rooms, to perform the transplants, making the length of the cycle an important factor; a study has shown that an improvement in length of more than 3 has no effect on the size of the exchange [28].

2.1.1 Kidney Exchange Problem (KEP)

A transplant, as we mentioned before, is the best option for persons with end-stage kidney disease. Patients that have a donor willing to donate may not be compatible due to blood type or positive cross-match incompatibilities. This then becomes on an incompatible patient-donor pair (PDP). The kidney exchange problem is established from a pool of PDPs, denoting with edges the possibility of compatibility between these pairs [18].

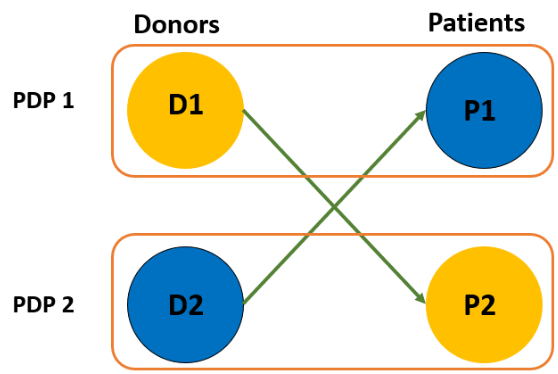

Figure 2.1: Cycle of length two of a kidney exchange.

An exchange, as mentioned before, is called a two-way exchange or 2-cycle kidney exchange when there are two incompatible pairs: PDP 1 and PDP 2 (Figure 2.1), where Donor 1 is compatible with Patient 2 and Donor 2 is compatible with Patient 1 and the pairs can exchange kidneys. Similarly, we can have situations with three-way exchanges among PDPs (see Figure 2.2).

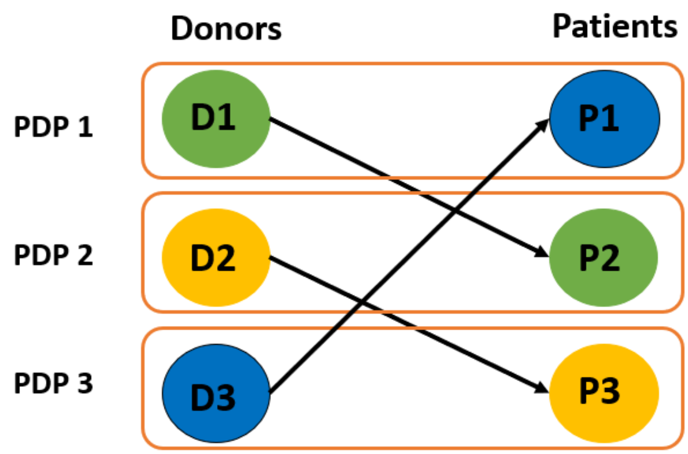

Figure 2.2: Cycle of length three of a kidney exchange.

The kidney exchange problem (KEP) is a well-known topic in different countries, deriving from the barter exchange, as we described before in this thesis. This problem can be seen as a graph, where the nodes are the agents or patients and donors, and the edges denote compatibility from a donor to a patient in another pair of patient-donor.

A cycle represents a possible exchange, in which each patient obtains a kidney from the next pair of patient-donor, and so on. The weight of a cycle is given by the sum of all the weights of all edges involved in the cycle, and the weight of an exchange is the sum of all the cycle weights involved in the exchange. The problem consists of finding a collection of cycle of length k or less that maximizes the total weighted sum. Note that when all weights are equal to one, the problem is equivalent to finding the largest amount of transplants among patients.

These cyclic exchanges lead to models allowing cycles only of length at most k; however, there is another type of exchange that allows for non-cyclic (or chain) exchanges. These are triggered by altruistic donors [26].

The non-directed donors (NDDs) or altruistic donors are persons with no interest or any benefit particularly that decided to donate a kidney developing a new response in the availability with the growing demand in organs needed [19]. Before kidney exchange programs arise, a NDD would donate his/her kidney to the top compatible patient in the waiting list. Nowadays, within the context of a kidney exchange program, PDPs are also involved in the exchange in such a way that the altruistic donor “starts” a chain exchange by donating to a PDP which in turns donates to another PDP and so on. The last PDP in the chain donates to the waiting list. This chain exchange is illustrated in Figure 2.3.

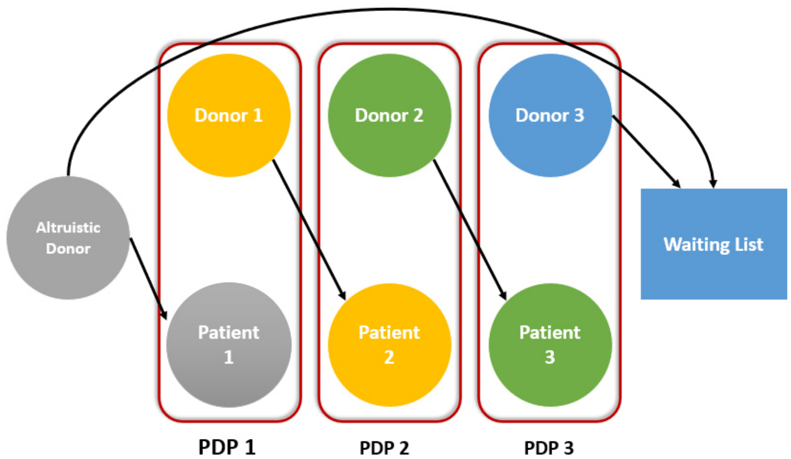

Figure 2.3: Chain exchange example.

Kidney pair donation has its issues. For instance, a study by Villa and Patrone [30] evaluates some mechanisms to show how some NND may be subject to possible manipulations from patients and donors and the misrepresentation of private pieces of information from these persons to motivate living donations for the kidney exchange problem. With the use of game theory and the use of a model, they measured the response of the model with complete information and with incomplete information to see how that impacts the compatibility between recipients and donors.

2.1.2 Kidney Exchange Program

A kidney exchange program can be controversial because of all the legislative barriers when an implementation of a program such as this is considered, especially for countries with a low rate of cadaver harvesting. A country that considers a kidney exchange program must face variables such as the acceptance of patients to enter the programs and his donors, and how patients can be included when they accepted.

According the practice standards in countries implementing kidney paired-donation programs [25], it is important to assess the psychological condition of every person involved in a transplant before any schedule takes place. Patients and donors must be fully aware of both the benefits and the risks of such operation, and the decision must be made willingly under mental stability conditions.

The first time that a kidney exchange program has been used as a concept to help or support programs for deceased donors in the USA is described by Rapaport [23]. Available programs cannot meet the demand for kidneys, and several studies about these programs have been conducted with the goal of presenting the maximum number of compatible transplants on the basis of the information about the patients, and waiting list used.

These days, there are studies on different approaches on how kidney exchange programs can be conducted more efficiently. As explained by Ashlagi et al. [4], as the kidney exchange program grows and becomes more important the roll of the hospital in the transplants also becomes an issue because more persons are involved in the care of patients and donors. The hospitals try to find the maximum number of transplants, but there is an incentive to find the matches inside the hospital. Different mechanisms might need to be employed for matches between different hospitals and for internal matches.

Chapter 3

Methodology

With a case study, we explore what effects a kidney exchange program can have and how it can help the society of the state in Nuevo León and in the country as a whole. Using real data of patients on the waiting list, such as blood type and age, we want to provide information about how transplants can be performed in each of the hospitals involved and what happens if the information about the patients on the waiting list is made public so that more matches can be made and more lives can be saved.

We try to show the impact of the implementation of a real kidney exchange program and give options about real matches between patients that are now on dialysis treatment and hoping for a better quality of life and a cheaper treatment.

3.1 The need of kidney Paired Donation Programs

The main problem in México is that, for some reason, the hospital institutions do not share their information among them. This causes that even if a patient is compatible with a donor from a different hospital, the transplant cannot be carried out because between the barrier of the institutions.

The state of Nuevo León has several hospital and private clinics, but not all of them are authorized to perform transplants. The largest and most renowned hospital in the state is the Dr. José Euleterio Gonzalez University Hospital.

In México, this focus on health care comes from recent interest on finding new forms to seek a solution to the organ demand that has been growing. In the last few years, between 1999 and 2009 only 20,154 kidney transplants were performed [12].

Other countries already run this type of programs to probe the reactions and the score results of patient-donor pairs registered in these programs [11]. Ross et al. [29] discuss how different factors can affect the benefits of the kidney exchange program and how the impact of each factor can be estimated.

On the other hand, in México, according to the annual report of the CENATRA from 2018, the first simultaneous transplant was realized on two incompatible PDPs was carried out in 2016 [9]. Other paired transplants followed [7, 6]. However, these matches came from isolated efforts, and not as a result of using KEP models. In México, there ir not any kidney paired donation program. In contrast, there are other countries where these type of programs are now operating bringing great benefits to many patients. This highlights the importance of this thesis, that addresses the idea of implementing a kidney paired donation program in Mexico aiming at saving more lives.

3.2 Main Methodology

Chapter 5 focuses on the proposed experiments and the results that we obtained in the case study discussed in this thesis. The order followed in this study is based on previously studied algorithms for solutions of a problem that is of vital importance for the country and the state.

First, for the experimentation, we need the waiting lists from diverse institutions and the corresponding procedures to obtain information about the patients, such as blood type and age of each patient. Then, to complete the information needed for the experiments, we simulated the information of the living donors, which was not given because of the confidentiality of this information, to obtain the donors of each person on the waiting list. Further details are given in Chapter 5.

For the next step of the experimental stage, an experimental design is set with the goal of investigating several issues and assessing the different KEP models. Experiments are run over a sample of randomly generated instances. The individual instances are solved using cycle-only or chain-and-cycle KEP models (described in Chapter 4) depending on the specific experiment.

Chapter 4

Formulations for the kidney exchange problem

Over the years, many different formulations for the kidney exchange problem have been proposed, incorporating different forms for its solutions combining cycles and chains or just using one of the forms for the exchanges. The most used one is the cycle formulation [5], in which the integer programming (IP) model is used only for cycles, with the nodes representing the patient-donor pairs. Another formulation previously proposed in the literature is the edge formulation [28], which assigns a decision variable to each of the edges or arcs of the generated graph.

Some other formulations are the extended edge formulation [10] and the partitioned edge formulation proposed in [24], in which different formulations for cycles exclusively and chains and cycles are examined, with the intention to explore whether this formulation can present a better and faster form for a solution to the kidney exchange problem so that more transplants can be included in the solution.

In addition, there are formulations that combine cycles, such as the formulation mentioned before, but that also involve chains in the solution, for example, the arc-based formulation [3], which uses a variable for both chains and cycles.

As we mentioned before, there are several formulations for this problem, and they have been elaborated and explored by many researchers. For the purposes of this thesis we use the two formulations proposed in [5] and [3] to confront the actual situation in México and give a wide picture of how the life expectation of people on waiting lists and on a dialysis treatment can be improved when transplants can be performed.

The use of the cycle formulation is with the intention to see how transplants can be done in situations where there are not altruistic donors as is commonly the case. Nevertheless, for contrasting purposes, we also consider chain-and-cycle KEP models with unlimited chain length.

4.1 Cycle formulation

The first formulation represents an alternative IP model used for the purposes of this thesis; we called it the cycle formulation [1], which uses only cycles in the solution. Let $\zeta(k)$ be the set of all cycles in G with a length of at most k. We assume that a cycle is an ordered set of arcs. Define a variable z_C for each cycle $C \in \zeta(k)$:

$$z_C = \begin{cases} 1 & \text{if cycle } C \text{ is selected for the exchange,} \\ 0 & \text{otherwise.} \end{cases}$$

Denote by $V(C) \subseteq V$ the set of edges that belong to cycle C. The model can be written as follows (where $w_C = \sum_{(i,j)\in C} w_{ij}$):

$$\text{Maximize} \sum_{C \in \zeta_k} w_C z_C \tag{4.1}$$

subject to

$$\sum_{C: i \in V(C)} z_C \leq 1 \qquad i \in V \tag{4.2}$$

$$z_C \in \{0,1\} \qquad C \in \zeta(k) \tag{4.3}$$

In the case of unitary weights, w_C equals the number of edges in C, i.e., the number of transplants associated with cycle C. The objective function (4.1) maximizes the weighted number of transplants. Constraints (4.2) ensure that every vertex is in at most one of the selected cycles (i.e., each donor may donate only one kidney, and each patient may receive only one kidney). Compared to the edge formulation [1], the difficulty is the exponential number of variables. The number of cycles can grow exponentially with k.

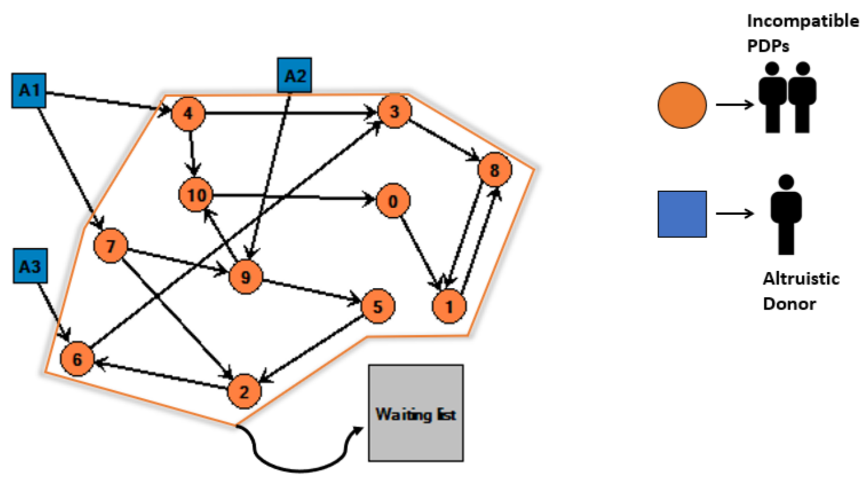

Figure 4.1: Example of a pool with PDPs and NDDs.

An interpretation of how this formulation works is given in Figure 4.1, in which we give an example of a pool that involves only patient-donor pairs for the implementation of the cycle formulation for this study.

Thus, if we give a solution to the implementation of the cycle formulation, we can see that in Figure 4.2 we find a cycle of length three for the pool example, as an illustration on how the formulation works and how it is going to be used in this study.

The natural conditions of this formulation can make it difficult to solve, such that a lot of computational effort might be needed. It is well known that the cycle-only model with no limit on k is solvable in polynomial time. However, the cases for k fixed, are NP-hard. Nevertheless, instances of reasonable size can be solved exactly by means of existing KEP models.

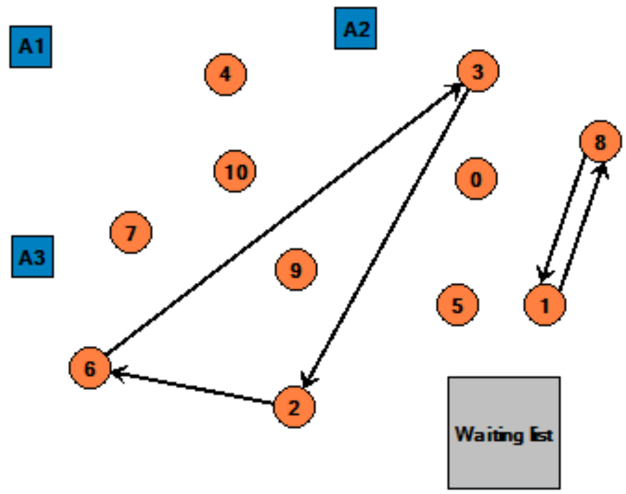

Figure 4.2: Example of solution with cycles of length 2.

4.2 Cycle-and-Chain Formulation

Now we describe the second model for solving the KEP, inspired by a solution to the price-collecting traveling salesman problem (PC-TSP) [3]. Recall that in the traveling salesman problem (TSP) one is given a list of cities and the cost of going between pairs of cities, and the goal is to find a cycle visiting each city exactly once at the minimum cost. In the PC-TSP, again one must find a cycle visiting each city at most once, but now one has the option of skipping some cities entirely and paying a penalty. Qualitatively, the PC-TSP problem is similar to the KEP in that one wants to find long paths in a graph without the need to visit every node.

The set V is partitioned into sets N (the NDDs) and P (the pairs of incompatible donors and patients). For $u; v \in V$, a directed edge from u to v in E indicates that the donor in node u is compatible with the patient in node v.

We introduce some notation. For each $v \in V$, let $\delta^-(v)$ be the edges pointing to v and $\delta^+(v)$ be the edges outgoing from v. Likewise, for a set of nodes $S \in V$, let $\delta^-(S)$ for each cycle C be of a length of at most k, and we introduce a new variable z_C that indicates whether we are using the cycle C.

Now, z_C is a variable for every feasible cycle C, and x_{ij} is a variable for edges in unbounded chains, defined as follows:

$$z_C = \begin{cases} 1 & \text{if cycle } C \text{ is selected for the exchange,} \\ 0 & \text{otherwise.} \end{cases}$$

$$x_{ij} = \begin{cases} 1 & \text{if edge } (i,j) \text{ is used in a chain,} \\ 0 & \text{otherwise.} \end{cases}$$

In addition to this, some auxiliary variables f_i^e and f_i^o for all $i \in V$ for the flow entering into i and the flow going out from i, respectively, are defined to simplify the formulation. Then, the PC-TSP-based formulation (PC-TSP) can be expressed as below:

$$\text{Maximize} \sum_{(i,j)\in E} x_{ij} w_{ij} + \sum_{C \in C_k} z_c w_c \tag{4.4}$$

subject to

$$\sum_{(i,j)\in E} x_{ij} = f_i^e \qquad i \in V \tag{4.5}$$

$$\sum_{(i,j)\in E} x_{ij} = f_i^o \qquad i \in V \tag{4.6}$$

$$f_i^o + \sum_{C\in\zeta_k(i)} z_C \le f_i^e + \sum_{C\in\zeta_k(i)} z_C \le 1 \quad i \in P \tag{4.7}$$

$$f_i^o \le 1 \qquad i \in N \tag{4.8}$$

$$\sum_{(j,m):j\in\bar{S},m\in S} x_{jm} \ge f_i^e \qquad S \subseteq P, i \in S \tag{4.9}$$

$$x_{ij} \in \{0,1\} \qquad (i,j) \in E \tag{4.10}$$

$$z_C \in \{0, 1\} \qquad\qquad C \in \zeta_k \tag{4.11}$$

The objective function (4.4) maximizes the weighted number of transplants between chains and cycles in the solution. Constraints (4.5) define the flow entering into each node, and constraints (4.6) represent the flow out of each node, such that the flow entering into and out of each node is the same regardless of whether a patient receives a kidney or not. In constraints (4.7), we establish that every pair in the solution must be in a cycle or in a chain and that the flow out of any node i must be at most the flow coming into the same node.

Chapter 5

Experimental work

This chapter presents the computational experiments aiming at assessing the potential impact of a kidney exchange program under various scenarios.

In the first part of the work, experiments associated with the cycle-only version of the KEP (model discussed in Section 4.1) are carried out. In particular, the following experiments are carried out:

1. Solving individual databases considering cycle-only models.
2. Solving combined databases considering cycle-only models.

In the first experiments, we solve each individual database using cycle-only models, chain-only models and cycle-and-chain models (with cycle cardinality limit set to $k = 2$ and 3) under no priorities (all objective weights equal to 1). In the second experiment, we assess the impact of having combined databases compared to individual databases, again, under no priorities (all objective weights equal to 1).

In the second part of the work, experiments associated with the chain-only and chain-and-cycle versions of the KEP (models discussed in Section 4.2) are carried out. In particular, the following experiments are carried out:

1. Solving individual databases considering chain-only models.

2. Solving individual databases considering chain-and cycle models.

3. Solving combined databases considering chain-only models.

4. Solving combined databases considering chain-and-cycle models.

All the experimentation was carried out on a workstation with Intel XEON processor at 3.4 GHz and 16 GB of RAM. The solution algorithms for solving the KEP models were made available by [13] and [3]. The first algorithm were compiled with the 1.7 Java compiler and 10.0.17763.0 C++ compiler and whenever necessary linked to CPLEX 12.7 using Concert Technology for Java and C++.

For the formulations of the solutions to the problem, two different algorithms of solutions for each model were used. For the cycle formulation, the algorithm developed by Dickerson [13] was used. For the chain-and-cycle formulation, the algorithm developed by Anderson et al. [3] was used. In particular, we use John Dickerson implementation of this algorithm, the one proposed for Anderson in 2015, was used.

5.1 Description of databases and test instances

Although we have complete patient information in each databases, for confidentiality reasons potential donor information is not available either for protecting the donor, or simply, because a patient has not donor yet. However, one the main objectives of this thesis is precisely to assess how these patients can be benefit from a potential kidney exchange program. To this end, we proceed to simulate donors for each patient following the blood type distributions and patient-donor relationship of the Mexican population. This type of studies have been carried out before, see for example Gentry et al. [15] for a study made in the American population and Herrera Medrano [16] for a study made in the Mexican population.

These are serious studies that take into account the blood type distribution, the proportion of each type of relationship between patient and donor (e.g., spouse, children, parent, etc.), the frequency of the alleles inherited by each child, and so on. The state institution brings the waiting list of the patients already on a waiting list or in dialysis treatment in that hospital. We use the following real-world databases facilitated by some state- and nation-wide institutions:

- San José Hospital (SJH): Comprised of 35 patients as of 14/Dec/2018.
- Dr. José Euleterio Gonzalez University Hospital (UH): Comprised of 15 patients as of 14/Dec/2018.
- Public institutions and small private hospitals in Nuevo León (SSNL): Comprised of 1086 patients as of 14/Dec/2018.
- Nation-wide information from Centro Nacional de Trasplantes (CENATRA): Comprised of 17365 patients as of 14/Dec/2018.

The hospitals and institutions mentioned before each provided a database of information about the patients including blood type, age, and sex and this information was used to generate the needed information of all the living donors participating in experiments and find the solutions to show the impact of the study of this thesis. Each database has different size. In each database we found relevant information about the patients, but the most important for our study is that of blood type.

The UH database stands out because among all the patients listed, there were only two present blood types (O and A), such that for the experiments with chains for this database we only used instances considering two different blood types for altruistic donors in the use of chains and ignored the other blood types because we did not find any chain as we started with an altruistic donor with a specific blood type.

For each experiment carried out, we use the same information of patients from the provided database, and we considered some parameters for the experimentation as discussed below:

- Number of pairs on matches are determined by the length of each database
  - 15 patients from the UH database
  - 35 patients from the SJH database
  - 1,086 patients from the SSNL database
  - 17,367 patients from the CENATRA database
- Length of the cycles for the cycle-only models is set to either 2 or 3.
- The length of the chains in chain-related models is unlimited.
- The weight w_{ij} in the KEP model objective function is set to 1, that is, we are looking at maximizing number of transplants.
- For the chain-related experiments, where at least one altruistic donor is needed, we consider only one altruistic donor per instance.

For the solution of both formulations we make use of exact algorithms to solve the problems proposed before for all the experimentation. For the first formulation we make use of the algorithm implementation proposed by Dickerson [13] and for the second formulation we use the Anderson implementation [3] to solve the problems, keeping in mind that we obtain the instance for the algorithms from the simulator [16].

For the database combination experiments, it is sought to show and evaluate the importance of open collaboration between the hospitals. We illustrate different cases by merging databases two at a time. For instance, we merge database A and B, and create one single combined instance. We solve this instance and compare its solution to that of the individual database solutions. By doing this, we can establish the importance of open collaboration between hospitals.

5.2 Special considerations for the CENATRA database

It is important to notice that the CENATRA database, with over 17,000 patients, is practically intractable. In other words, the KEP models can not be solved with an instance of this size. In addition, it is also very unrealistic to think that each of the over 17,000 patients will bring a donor. Therefore, we generate instances taking a proportion of the total. For example, we can generate an instance of size 10% of the total by randomly choosing patients from the whole database until the desired number is achieved.

With these guidelines we created 20 different instances for each size that goes from 10% to 30% of the CENATRA database size.

5.3 Experimental Results

In this section, we present the results, analysis, and discussion of each of the experiments carried out. Section 5.3.1 presents the results related to cycle-only models. Sections 5.3.2 and 5.3.3 present the results related to chain-only and chain-and-cycle models, respectively.

5.3.1 Experiments considering cycle-only models

For each of the databases we solve the cycle-only models for two different cases: cycles of length 2 and 3, respectively. It is assumed each patient in the database has a living donor and therefore participates in the exchange. Each of the Figures 5.1 to 5.7 shows the number of transplants in the vertical axis (optimal value of the objective function) for the two different models, shown in the horizontal axis. Recall that 4 instances are solved for each model.

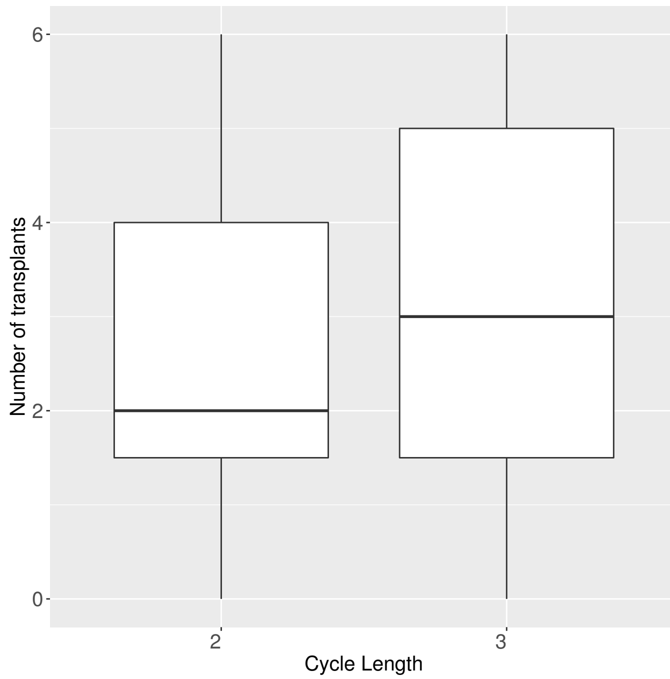

Figure 5.1: Results for the UH database ($n = 15$) for cycle-only models.

The results for the UH database are shown in Figure 5.1. As we can see in Figure 5.1, when the length of the cycle is fixed at 2 the average number of transplants performed is 2.8 out of the 15 pairs used. When the length of the cycle grows, as an expected behavior, the number of transplants performed increases and we observe that the average number of transplants is 3.6 when the length of the cycle is fixed at 3 for this database.

Figure 5.2 shows the results for the SJH database, with 35 patients. The summary of average results is displayed in Table 5.1. It is observed first, as in the previous experiments, that the average number of transplants when $k = 2$ and $k = 3$ is 10.0 and 12.65, respectively. This is consistent with the previous experiments. Furthermore, as we allow more patients to participate in the exchange, the proportion of the total also increases. That is, in the previous data set, on average, 2.8 out of 15 were benefited under the 2-cycle model, representing 18.6% of the total, whereas, for this data set, on average, 10 out of 35 patients were benefited, representing 28.6%

of the total. The same behavior is observed for the $k = 3$ models.

Table 5.1: Average number of transplants for models with cycle length of 2 and 3.

Number of patients	Cycle length	Database	Average number of transplants	Fraction of total
15	2	UH	2.8	18.66%
35		SJH	10.0	28.57%
1086		SSNL	420.0	38.67%
1136		CENATRA	445.5	39.21%
15	3	UH	3.6	24.00%
35		SJH	12.7	36.14%
1086		SSNL	453.2	41.73%
1136		CENATRA	480.6	42.30%

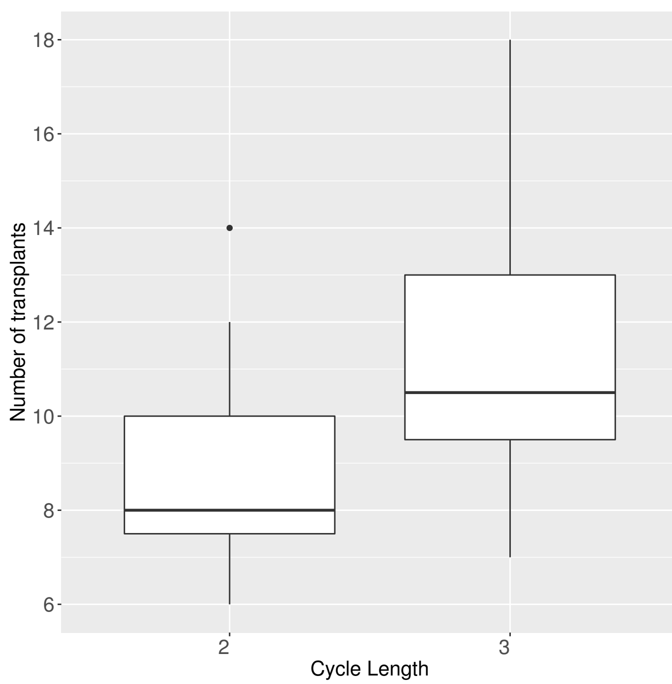

Figure 5.2: Results for the SJH database ($n = 35$) for cycle-only models.

In the following experiment, we attempt to show how collaboration between hospitals may be beneficial to patients. To this end, we now combine two of the individual databases into one (called the combined databases) and solve the problem for both $k = 2$ and $k = 3$ cases. The idea is to compare the results of the combined instance with those of the individual databases.

The results for the $k = 2$ and $k = 3$ cases are shown in Figure 5.3 and Figure 5.4, respectively. Again, the vertical axis indicates the number of transplants, and the horizontal axis shows the four different cases: (a) UH individual database, (b) SJH individual database, (c) sum of (a) and (b), and (d) UH+SJH combined database.

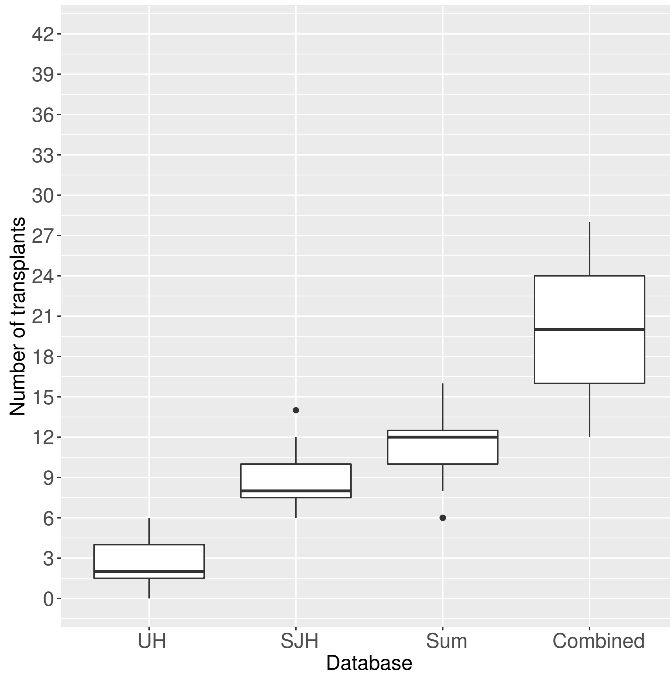

Figure 5.3: Comparison of individual and combined database (50 patients) for cycle-only models of length 2.

As we can see from Figure 5.3 and 5.4, the impact is significant. On average, the optimal number of pairs found for transplantation in the combined database is considerably larger than that of the sum of the optimal individual databases. This is observed for both cases, $k = 2$ and $k = 3$. Table 5.2 and 5.3 show the same results for $k = 2$ and $k = 3$, respectively, but itemized by each individual instance. In each table, the row indicates the instance solved and the columns indicate the case being solved. The last column indicates the relative improvement obtained by solving the combined database with respect to the sum of the optimal solution of the individual databases. As we can see from Table 5.2 and 5.3, an average relative improvement of 100% and 144% is observed. This clearly shows that collaboration between hospitals by sharing their databases for a common good yields many more patients being benefited.

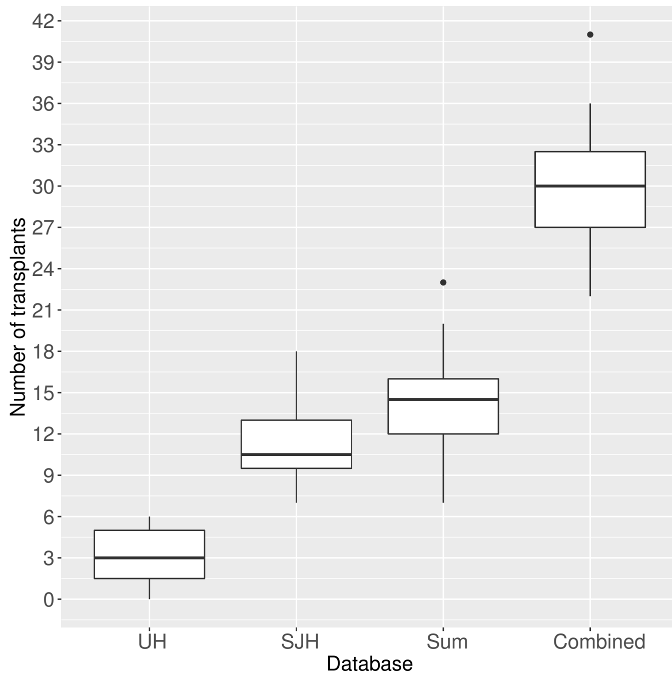

Figure 5.4: Comparison of individual and combined database (50 patients) for cycle-only models of length 3.

Another interesting observation, as indicated in the last column of both tables, is that all instances, but one, showed some improvement when using the combined database. For all others, at least a 20% improvement was observed. The reason for this is that the combined compatibility graph contains many edges between the two individual graphs. This produces a significant number of new feasible solutions that that of the individual databases. Therefore, when the combined graph is solved, more cycles among individual graphs can be found.

Another interesting result occurs in the 2-cycle instances. From Table 5.2, instances 9, 10, and 17, when solved for the UH database obtained zero pairs. That is, it was not possible to find any 2-length cycle in each of those instances. However, when these instances were solved by combining them with the SJH database, it was possible to match many patients from the UH database with some of the SJH

Table 5.2: Comparison of individual and combined database (50 patients) for cycle-only models of length 2 by individual instance.

Instance	UH	SJH	UH + SJH	Combined	Improvement (%)
1	2	10	12	20	66.66
2	4	10	14	14	0.00
3	4	6	10	24	140.00
4	2	8	10	12	20.00
5	5	6	8	14	24.00
6	2	12	14	16	14.28
7	2	14	16	20	25.00
8	2	8	10	14	40.00
9	0	6	6	26	333.33
10	0	10	10	28	180.00
11	2	10	12	24	100.00
12	4	8	12	24	100.00
13	2	8	10	18	80.00
14	0	6	6	18	200.00
15	4	10	14	16	14.28
16	0	12	12	12	0.00
17	0	6	6	26	333.33
18	4	8	12	22	83.33
19	2	10	12	18	50.00
20	2	6	8	20	150.00
				Average	100.08

Table 5.3: Comparison of individual and combined database (50 patients) for cycle-only models of length 3 by individual instance.

Instance	UH	SJH	UH + SJH	Combined	Improvement (%)
1	3	11	14	34	142.85
2	6	14	20	24	20.00
3	5	7	12	30	150.00
4	2	10	12	25	108.33
5	6	10	16	31	93.75
6	3	13	16	29	81.25
7	5	18	23	25	8.69
8	3	10	13	22	69.23
9	0	7	7	41	485.71
10	0	12	12	32	166.66
11	3	13	16	30	87.50
12	5	10	15	36	140.00
13	3	11	14	29	107.14
14	0	7	7	30	328.57
15	5	12	17	28	64.70
16	0	15	15	27	80.00
17	0	8	8	34	325.00
18	5	10	15	34	126.66
19	3	13	16	27	68.75
20	2	8	10	32	220.00
				Average	143.74

database resulting in a significant increase.

Finally, in Figure 5.5 we show a comparison between 2-cycle and 3-cycle models under each of the four previously discussed cases. In the figure, the horizontal axis indicates: (a) UH database, (b) SJH database, (c) sum (a)+(b), and (d) combined data set, and vertical axis show the number of transplants. As we can see, the cycle length plays an important roll as well, thus it is strongly recommended, when possible, try to seek 3-cycle exchanges. This may not be always possible due to hospital limitations, though.

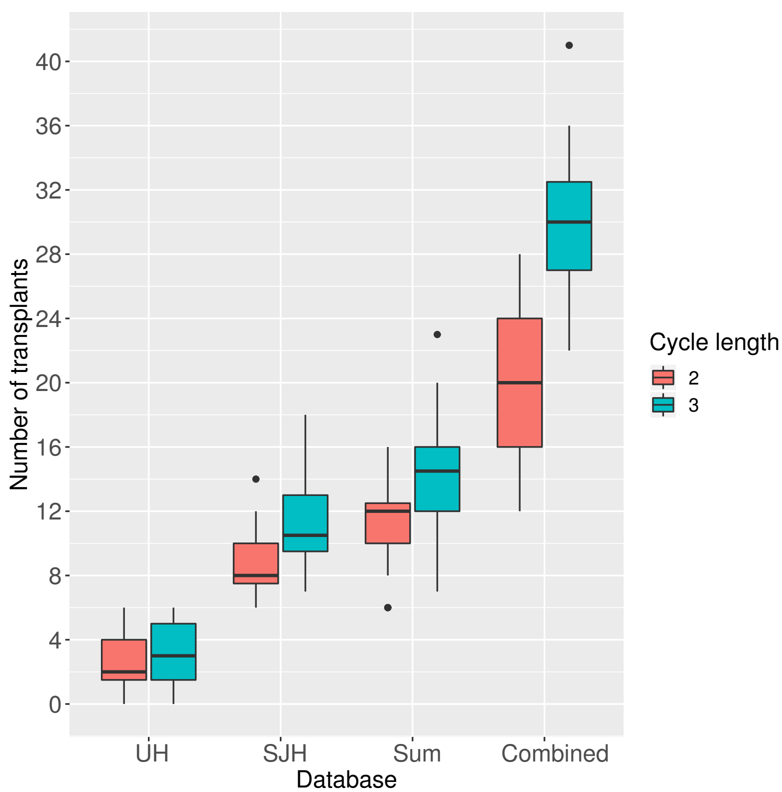

Figure 5.5: Comparison between models with cycles of length 2 and 3 on individual and combined databases.

We now present the results for the NL database with 1086 patients. In this experiment, given the number of patients is very high, we solved the instances for several donor to patient ratio values. Figure 5.6 shows the results, where the horizontal axis indicates the donor to patient ratio. For instance, the 10% column means that instances were solved assuming 10% of donors, that is instances of size 108 were solved.

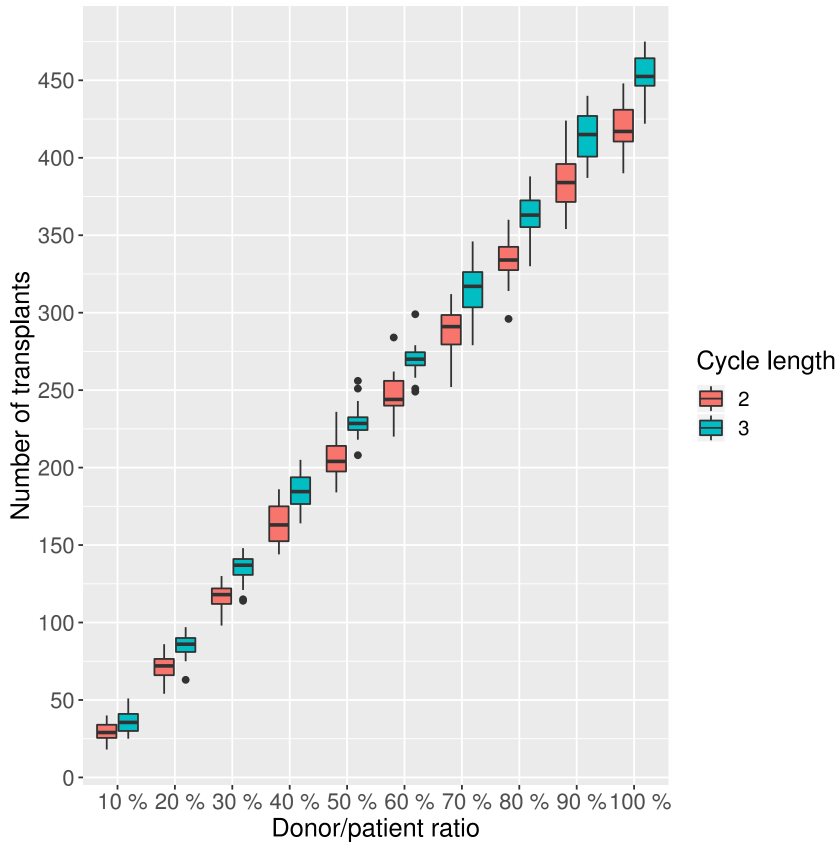

Figure 5.6: Comparison between models with cycles of length 2 and 3 and different donor to patient ratio on the NL database.

From this figure, we can see the possible increase in the total number of transplants as the donors show an interest in a kidney exchange program, and this is represented in donor percentage. As we can see from the figure, there is an evident contrast in the extreme cases. For example, in the 10% donor/patient ratio column (that is, instance of size 108), we have as a result an average of 29.5 matches, whereas in the 100% donor/patient ratio column (that is, instance of size 1086), we have on average 420 matches. The former represents around 27% of the total and the latter represents 38% of the total. Table 5.4 shows the average results for each combination.

The same behavior is observed when looking at the 3-cycle instances. On average, 36.0 and 453.2 matches are found for the 10% and 100% donor/patient ratios, respectively, representing 33% and 42% of the total, respectively.

We now repeat the same experiment but using a combined data set consisting of NL, UH, and SJH databases, that is, 1136 pairs. Results are displayed in Figure 5.7.

The use of donor to patient ratio allows us to clearly see the advantage gained when more donors are willing to participate in this type of exchange programs.

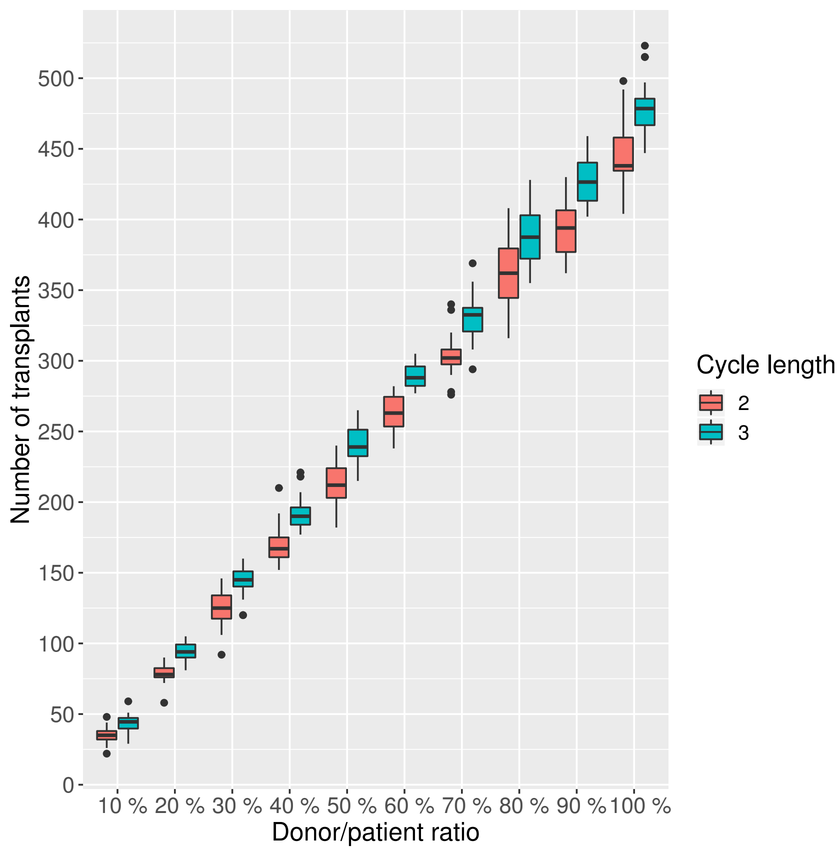

Figure 5.7: Comparison between models with cycles of length 2 and 3 and different donor to patient ratio on the augmented database (NL + UH + SJH, 1136 pairs).

As we can see from Figure 5.7, the results are very similar to those from the previous experiment. Allowing cycles of size 3 results in more matches and therefore

Table 5.4: Comparison between models with cycles of length 2 and 3 and different donor to patient ratio on the NL database based on the average number of transplants.

Donor/patient ratio (%)	Average number of transplants	
	$k = 2$	$k = 3$
10	29.40	36.05
20	71.60	85.00
30	115.80	134.70
40	163.70	184.35
50	206.80	229.75
60	246.70	269.65
70	287.90	315.50
80	334.60	363.50
90	384.60	412.65

should be pursued. From these last two experiments we can conclude that it is very important to motivate a donation culture among the population. The more people willing to participate the more people can be helped.

In our last experiment in this section, we carry out a similar study as that of the previous experiment using this time the nation-wide CENATRA database. Again, because this database has 17,365, we run a few experiments setting the donor to patient ratio to 10%, 20% and 30%. This last instance has a size of 17,365 patients, which is about the size of the KEP model that can be solved by the optimization algorithm. The results are presented in Figure 5.8.

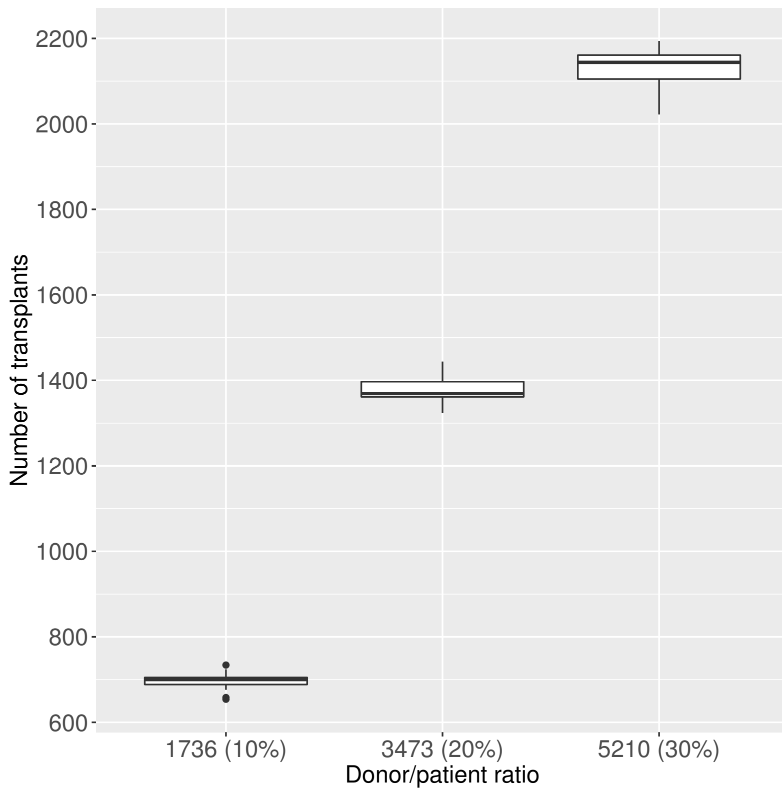

Figure 5.8: Results of models with cycles of length 2 and different donor to patient ratio on the nation-wide CENATRA database (17,365 patients).

As a general conclusion from these last experiments, we can see that even a small participation of 10% (involving 1,736 donors) results in 700 matches, which is very good. As the donor/patient ratio increases so does the number of matches.

5.3.2 Experiments considering chain-only models

In this section, we carry out some experiments considering chain-only models. Recall, that kidney exchange based on chains arises when there are altruistic donors. To this end, in our problem instances we are assuming there is only one altruistic donor. This donor can have any blood type,, which will be explained in each experiment. Clearly, the more altruistic donors we have, the more chains that can be formed.

However, for the purposes of these experiment only one altruistic donor per instance is considered.

In the first experiment, we solved the chain-only model for each possible altruistic donor blood type (that is, four cases) in the UH database. The figure only includes the result for blood type O and A, because no chains were found in the other two cases (blood type B and AB). The results are shown in Figure 5.9.

As can be seen from Figure 5.9, more matches are found when the altruistic donor has blood type O as compared with blood type A. This is somehow explained by the fact that a blood type donor is compatible with types A, B, AB and O, whereas blood type A is only compatible with type A and AB. Therefore, there are more chances of finding paths if the altruistic donor has type O.

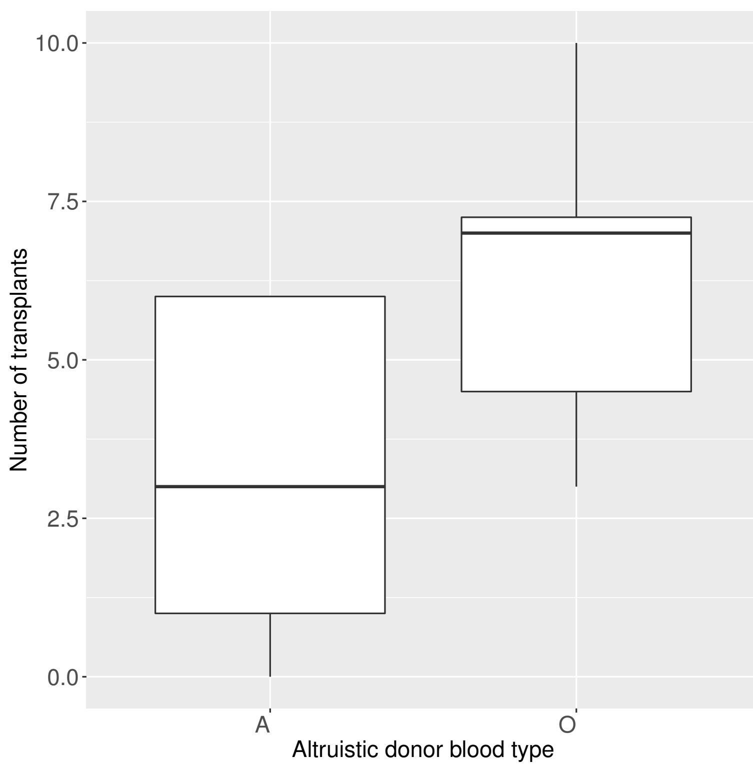

Figure 5.9: Results for the UH database ($n = 15$) for the chain-only model.

We repeat the same experiment, but this time using the SJH database. The results are shown in Figure 5.10, where the horizontal axis shows the altruistic donor blood type. Type AB is not shown because there are not compatible pairs.

As can be seen, the average number of matches is higher when altruistic donor is of blood type O, which is consistent with the previous experiment. It is also interesting to see how the average match pattern changes as a function of the altruistic donor blood type. The variance is a lot higher when the altruistic donor has blood type A.

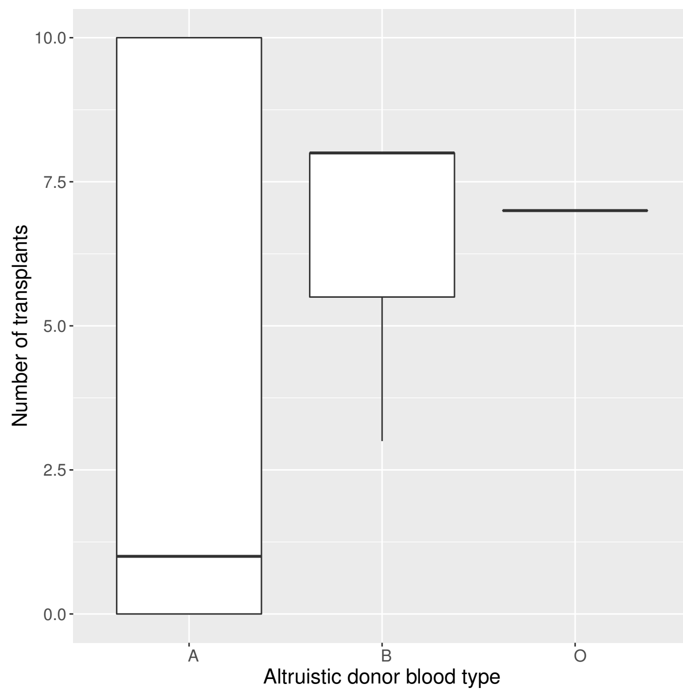

Figure 5.10: Results for the SJH database ($n = 35$) for the chain-only model.

In the following experiment, we solve the UH, SJH and combined (UH+SJH) databases under the chain-only model assuming an altruistic donor of blood type A. The results of the individual instances are shown in Table 5.5.

Table 5.5: Comparison of individual and combined database for chain-only models with altruistic blood type A by individual instance.

Instance	UH	SJH	UH + SJH	Combined	Improvement (%)
1	1	6	7	7	0.00
2	3	6	9	10	11.11
3	6	0	6	7	16.66
4	3	1	4	7	75.00
5	5	6	11	11	0.00
6	6	6	12	13	8.33
7	6	0	6	7	16.66
8	1	6	7	7	0.00
9	4	6	10	11	10.00
10	1	6	7	7	0.00
11	1	0	1	1	0.00
12	6	6	12	12	0.00
13	3	0	3	7	133.33
14	2	6	8	9	12.50
15	6	6	12	12	0.00
16	3	0	3	7	133.33
17	0	1	1	1	0.00
18	6	6	12	13	8.33
19	0	1	1	7	600.00
20	0	0	0	7	700.00
				Average	86.26

In the following experiment, we solve the UH, SJH and combined (UH+SJH) databases under the chain-only model assuming an altruistic donor of blood type B. The results of the individual instances are shown in Table 5.6.

Table 5.6: Comparison of individual and combined database for chain-only models with altruistic blood type B by individual instance.

Instance	UH	SJH	UH + SJH	Combined	Improvement (%)
1	0	6	6	6	0.00
2	0	6	6	6	0.00
3	0	6	6	6	0.00
4	0	6	6	6	0.00
5	0	5	5	6	20.00
6	0	6	6	6	0.00
7	0	6	6	6	0.00
8	0	6	6	6	0.00
9	0	6	6	6	0.00
10	0	6	6	6	0.00
11	0	6	6	6	0.00
12	0	5	5	6	20.00
13	0	3	3	6	100.00
14	0	6	6	6	0.00
15	0	6	6	6	0.00
16	0	6	6	6	0.00
17	0	6	6	6	0.00
18	0	6	6	6	0.00
19	0	6	6	6	0.00
20	0	6	6	6	0.00
				Average	7.00

As we can see from Table 5.6, the results were not as good as expected due in part to the fact that only the SJH database reported patients with this blood type. In addition, the combined data set has larger cardinality, therefore the proportion of matches found is observed relatively modest when compared to other blood types.

5.3.3 Experiments considering chain-and-cycle models

In this section, we carry out some experiments considering chain-and-cycle models. This represents the higher flexibility as both paired-exchange and chain-exchange are allowed. Again, as in the previous sections we are assuming there is only one altruistic donor per instance.

For these experiments we use the same instances used in the previous section. A critical issue to investigate is the possible effect we might find on the final solutions when allowing both chains and cycles.

As we will see in Figure 5.11, it was observed that the databases behave in the same way for the different blood type of the altruistic donor. Thus, the altruistic donor blood type does not seem to play a significant role in the individual databases. However, observations are different when solving the combined database.

In the following experiments, we present first results from instances where the altruistic donor has blood type O. Unlimited size chains, and cycle length of size 2 and 3 are considered. This is followed by results for altruistic donor blood type A, B, and AB. In this case, it was possible to obtain and report results for blood type AB as the number of matches is also influenced by the formation of cycles.

Figure 5.11 displays the results obtained on the UH database. As can be seen, results are better when altruistic donor has type O, which is to be expected given type O is a universal donor, thus more chances to find matches. Figure 5.12 displays the results obtained on the UH database. Table 5.7 displays a summary of the results. As can been seen from the table, the results from the cycle-and-chain models are significantly better than those from cycle-only models. This happens because the former models allow for more people to get involved and therefore have a better chance to find a match.

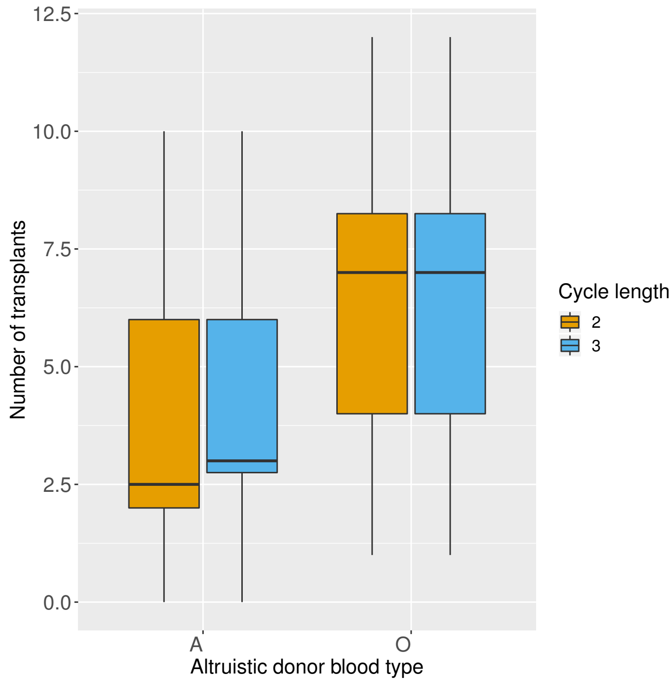

Figure 5.11: Comparison using different blood type in the altruistic donor and cycle length for the UH.

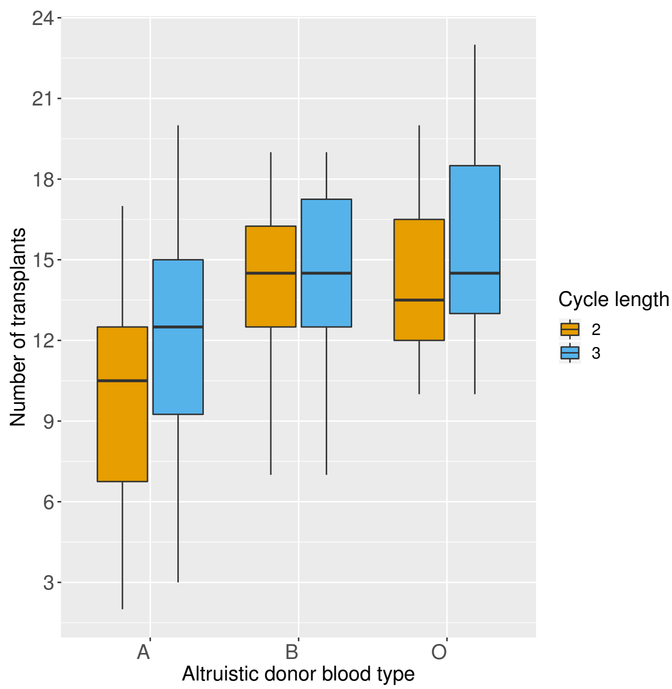

Figure 5.12: Comparison using different blood type in the altruistic donor and cycle length for the SJH.

Table 5.7: Comparison of individual and combined database for chain-and-cycle models with altruistic blood type A by individual instance.

	$k = 2$					$k = 3$			
Instance	UH	SJH	UH+SJH	Combined	Improvement (%)	UH	SJH	UH+SJH	Combined	Improvement (%)
1	2	8	10	36	260.00	2	11	13	43	230.76
2	4	12	16	35	118.75	4	13	17	39	129.41
3	10	4	14	33	135.71	10	5	15	38	153.33
4	2	12	14	26	85.71	3	14	17	33	94.11
5	5	17	22	24	9.09	5	19	24	32	33.33
6	6	12	18	38	111.11	6	16	22	41	86.36
7	1	2	3	30	900.00	1	3	4	38	850.00
8	8	14	22	40	81.81	8	15	23	44	91.30
9	2	5	7	32	357.14	3	6	9	38	322.22
10	2	10	12	40	233.33	3	12	15	45	200.00
11	0	14	14	28	100.00	0	15	15	37	146.66
12	2	10	12	28	133.33	3	12	15	34	126.66
13	2	16	18	18	0.00	3	20	23	24	4.34
14	0	7	7	18	157.14	0	10	10	28	180.00
15	2	7	9	12	33.33	2	12	14	26	85.71
16	6	11	17	28	64.70	6	13	19	34	78.94
17	3	6	9	38	322.22	4	7	11	41	272.72
18	3	11	14	22	57.14	3	13	16	34	112.50
19	7	2	9	32	255.55	7	3	10	38	280.00
20	8	16	24	46	91.66	8	17	25	48	92.00
				Average	175.38				Average	178.52

Figures 5.13 and 5.14 display the results for the chain-and-cycle models of length 2 and 3, respectively, when the altruistic donor has blood type A. Comparing these with the ones in Figure 5.3 and 5.4 we see that the average obtained is 31.2 and 35, for the chain-and-cycle models using a cycle length of 2 and 3, respectively and average for the cycle-only model is 19.5 and 30 with cycle length of 2 and 3 respectively.

As can be seen in Figure 5.13 and Figure 5.14, we observe that the results for the individual databases are similar; however, the number of matches significantly grows when solving the combined database. The average number of transplants found in the combined data set is 30.2 and almost 40, for the models with cycle length of 2 and 3, respectively.

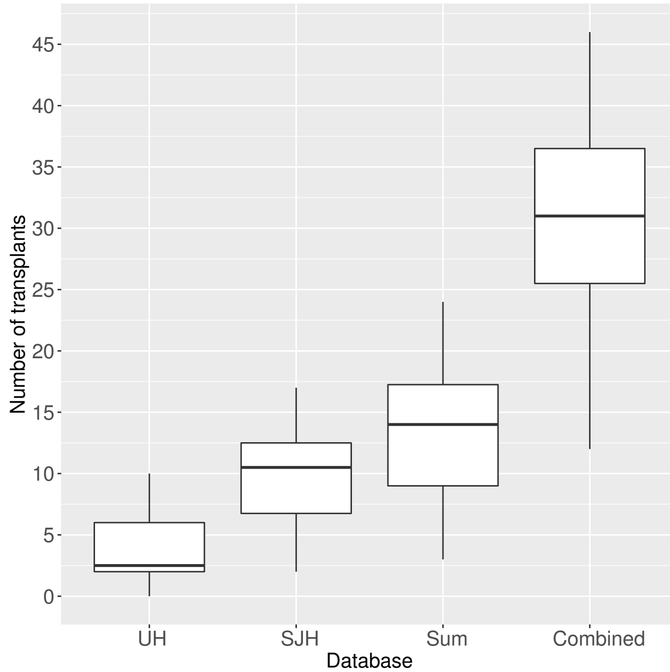

Figure 5.13: Comparison of individual and combined database for chain-and-cycle models ($k = 2$) with altruistic blood type A.

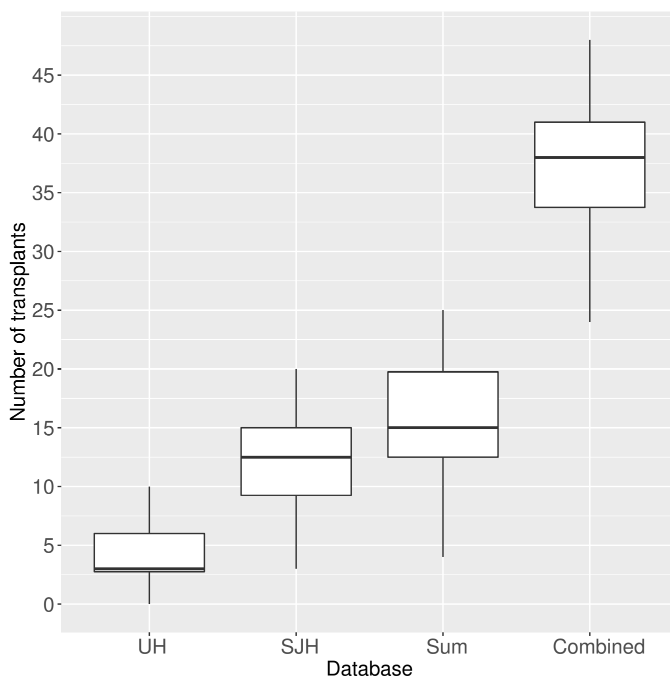

Figure 5.14: Comparison of individual and combined database for chain-and-cycle models ($k = 3$) with altruistic blood type A.

Next, we present the results obtained when considering an altruistic donor of blood type B. Figure 5.15 and Figure 5.16 show the results for the individual and combined data sets under $k = 2$ and $k = 3$, respectively. Table 5.8 displays the same results itemized by individual instance. As we can see from Figure 5.15, the results are similar to the ones obtained with an altruistic donor with blood type A. Contrasting with the previous experiment (blood type A), we can see that for instance, the average number of matches found for the sum of both databases under blood type A (Table 5.7) is 30.2 for $k = 2$ and 36.75 for $k = 3$. For this new experiment, this average (Table 5.8) improves to 34.7 and 41.4, respectively.

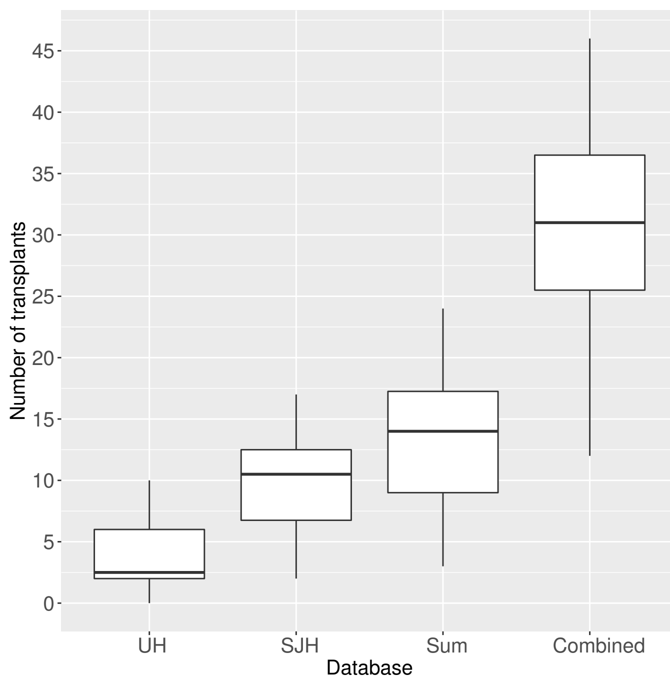

Figure 5.15: Comparison of individual and combined database for chain-and-cycle models ($k = 2$) with altruistic blood type B.

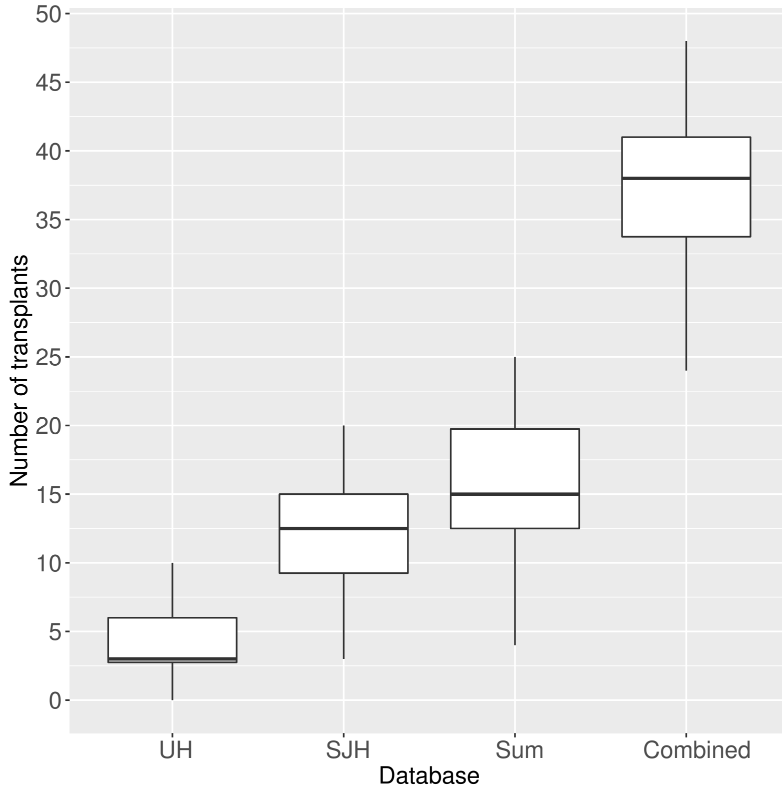

Figure 5.16: Comparison of individual and combined database for chain-and-cycle models ($k = 3$) with altruistic blood type B.

As we can see in the Table 5.8, the use of the combined database consistently outperforms the sum of individual databases for both cases ($k = 2$ and $k = 3$). Furthermore, a better average improvement was observed for the case $k = 3$ when compared with the case $k = 2$.

Table 5.8: Comparison of individual and combined database for cycle-and-chain models with altruistic blood type B by individual instance.

	$k = 2$					$k = 3$				
Instance	UH	SJH	UH+SJH	Combined	Improvement (%)	UH	SJH	UH+SJH	Combined	Improvement (%)
1	3	7	10	38	280.00	3	8	11	42	281.81
2	0	7	7	34	385.71	0	8	8	40	400.00
3	2	8	10	38	280.00	3	10	13	42	223.07
4	6	14	20	34	70.00	8	14	22	46	109.09
5	2	8	10	20	100.00	2	9	11	31	181.81
6	2	12	14	28	100.00	2	12	14	36	157.14
7	2	14	16	32	100.00	2	15	17	43	152.94
8	4	16	20	32	60.00	5	17	22	42	90.90
9	2	6	8	39	387.50	3	6	9	45	400.00
10	8	3	11	38	245.45	9	4	13	47	261.53
11	0	16	16	40	150.00	0	17	17	46	170.58
12	2	15	17	34	100.00	2	16	18	41	127.77
13	4	16	20	45	125.00	5	17	22	47	113.63
14	2	4	6	34	466.66	2	7	9	40	344.44
15	0	20	20	32	60.00	0	20	20	39	95.00
16	0	8	8	34	325.00	0	9	9	42	366.66
17	4	12	16	32	100.00	4	15	19	35	84.21
18	6	20	26	26	0.00	8	22	30	37	23.33
19	2	12	14	42	200.00	3	13	16	44	175.00
20	0	26	26	42	61.53	3	26	29	43	48.27
				Average	179.84				Average	190.36

Finally, the last set of experiments consider an altruistic donor of blood type AB. Figure 5.17 and Figure 5.18 show the results for the individual and combined data sets for $k = 24$ and $k = 3$, respectively. Table 5.9 displays the instance by instance results. From Figures 5.17 and 5.18, the first observation is that, as observed before, using the combined data set is significantly better than using the individual data sets. Thus, collaboration between hospitals is strongly encouraged. We can also see that allowing cycles of length 3 improves the solution by 1.43% with respect to allowing cycles of length 2.

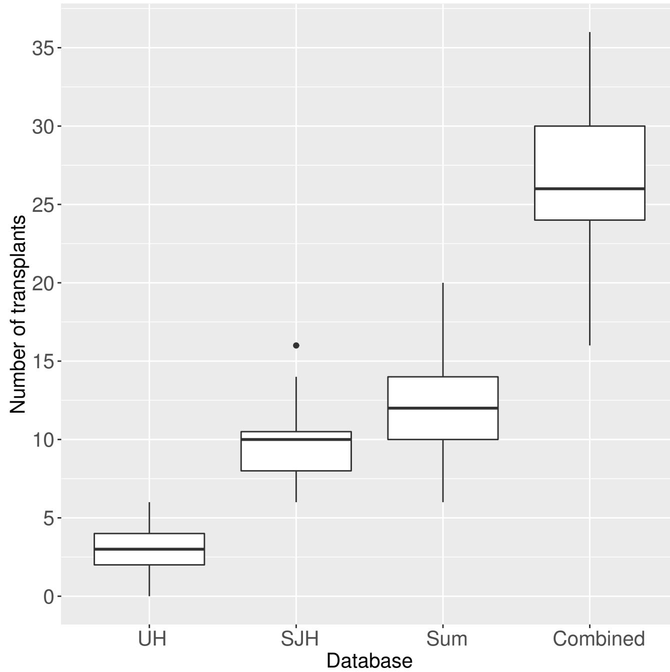

Figure 5.17: Comparison of individual and combined database for chain-and-cycle models ($k = 2$) with altruistic blood type AB.

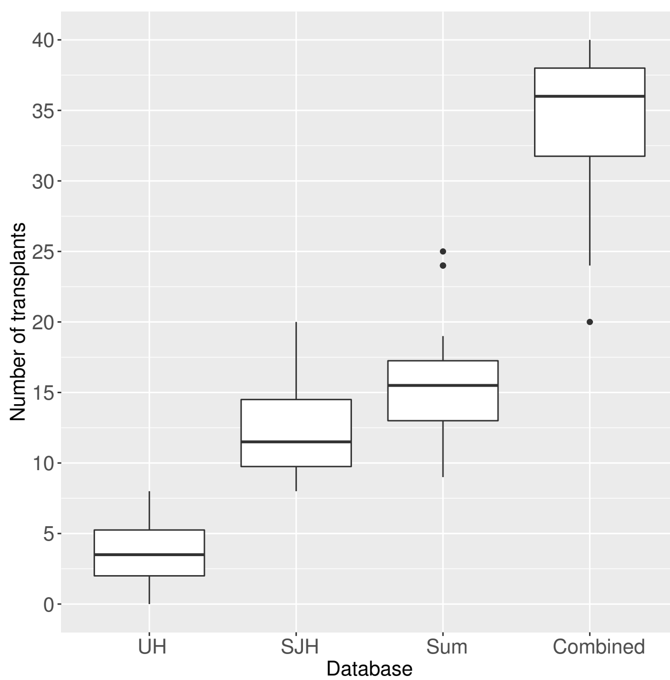

Figure 5.18: Comparison of individual and combined database for chain-and-cycle models ($k = 3$) with altruistic blood type AB.

Table 5.9: Comparison of individual and combined database for cycle-and-chain models with altruistic blood type AB by individual instance.

	$k = 2$					$k = 3$				
Instance	UH	SJH	UH + SJH	Combined	Improvement (%)	UH	SJH	UH + SJH	Combined	Improvement (%)
1	4	10	14	24	71.42	5	12	17	35	105.88
2	0	10	10	26	160.00	0	13	13	31	138.46
3	4	8	12	30	150.00	4	9	13	38	192.30
4	2	10	12	16	33.33	3	11	14	20	42.85
5	4	8	12	24	100.00	6	10	16	32	100.00
6	0	6	6	20	233.33	0	9	9	26	188.88
7	2	6	8	30	275.00	3	8	11	38	245.45
8	0	10	10	36	260.00	0	16	16	40	150.00
9	2	10	12	16	33.33	2	14	16	24	50.00
10	4	14	18	32	77.77	6	18	24	37	54.16
11	0	12	12	32	166.66	3	16	19	36	89.47
12	4	10	14	26	85.71	6	11	17	36	111.76
13	4	10	14	28	100.00	4	10	14	38	171.42
14	4	10	14	30	114.28	6	12	18	36	100.00
15	2	8	10	16	60.00	2	11	13	25	92.30
16	2	12	14	26	85.71	2	13	15	35	133.33
17	2	6	8	24	200.00	3	8	11	38	245.45
18	4	16	20	30	50.00	5	20	25	37	48.00
19	6	12	18	32	77.77	8	16	24	38	58.33
20	4	8	12	26	116.66	4	9	13	34	161.53
				Average	122.55				Average	123.98

Chapter 6

Conclusions

6.1 Main contributions and conclusions

This thesis illustrates the application of a combinatorial optimization problem in the health care sector. The kidney exchange problem (KEP) has a remarkable importance due to the potential impact that can have on procuring kidney transplants to needy patients. This is a clear example of how operations research tools and methodologies can help people have a better quality of life, and can help government and health care providers spend their limited resources wisely.

Kidney exchange programs have been successfully implemented in other countries. In México, we have no such programs. Kidney-paired exchange has a tremendous potential for development in México. The main contribution of this thesis is to show this potential and impact, by carrying out several meaningful experiments under different conditions. It was shown how the number of people that could be benefited by kidney exchange could be very large.

The presented results are very promising. Either in cycle-only models or models involving chains, many people could be helped by kidney paired-donation. An interesting observation found was that involving altruistic donor triggers the addition of chains, resulting in even more matches found. In particular, it was found that the numbers of transplants for the experiments involving altruistic donor with blood type O was better when compared to other blood types.

Another very interesting finding is that we also show how collaboration between hospitals and institutions, sharing their databases, could also significantly increase the number of matches. Therefore, collaboration between hospitals is strongly encouraged. In particular, we showed that finding the optimal number of transplants in the UH and SJH combined database was significantly larger than the sum of both databases optimized individually. This behavior was conclusively observed for all types of models (cycle-only and chain-related models). This, of course, can have a tremendous impact should a kidney exchange program be implemented at any regional level (city-, state-, or nation-wide).

The results obtained in this thesis can certainly be used as a basis for developing and establishing a kidney exchange program in México. The main idea behind this study is to motivate a kidney exchange program implementation due to the fact that no such program exists as of today in México.

6.2 Future work

Naturally, this type of problem has many avenues for further research. While this study focuses on applying optimization tools to address a kidney exchange problem, there are certainly other areas in organ donation that can be subject to study under the operations research umbrella. For instance, there are recent studies addressing liver transplants from the operations research perspective [22, 31], which can be further investigated in the specific Mexican situation.

In terms of kidney paired-donation through operations research techniques, one could enhance the study in several forms. For instance, doing state-by-state analysis with other state databases, or incorporating other health care institutions into the equation could be worthy. Now, in this particular study we are assuming every pair is equal, and therefore all weights in the objective function were assumed to be equal to one. However, it could be worthwhile to investigate how the assignment pattern changes as customer priorities are considered, that is, setting weights to different values.

In this study, we are assuming deterministic models; however, there have also been recent studies that consider uncertainty into the decision process [14, 17]. It would be interesting to carry out a study considering this aspect as well.

From a practical stand-point, a natural next step for an actual implementation of a kidney exchange program is to investigate the legal matters involved in a project of this sort. We have shown we have the technology, the models, and the algorithms for solving KEPs. Now, proper authorities must now research and set the basis for a feasible developing of a kidney exchange program.

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Resumen autobiográfico

Yessica Reyna Fernández

Candidato para obtener el grado de

Maestría en Ciencias en Ingeniería de Sistemas

Universidad Autónoma de Nuevo León

Facultad de Ingeniería Mecánica y Eléctrica

Tesis:

Potential Impact of Implementing a Kidney Exchange Program in Mexico: Case Studies from Mexican Databases

Nací el 27 de mayo de 1994 en Monterrey, Nuevo León, México. Mis padres son Ma. Cleofas Fernández Rámirez y Juan Manuel Reyna Alvarado. A los 17 años de edad ingresé a la Universidad Autónoma de Nuevo León para empezar mis estudios de licenciatura. A los 23 años de edad me titulé con el grado de Licenciado en Matemáticas.